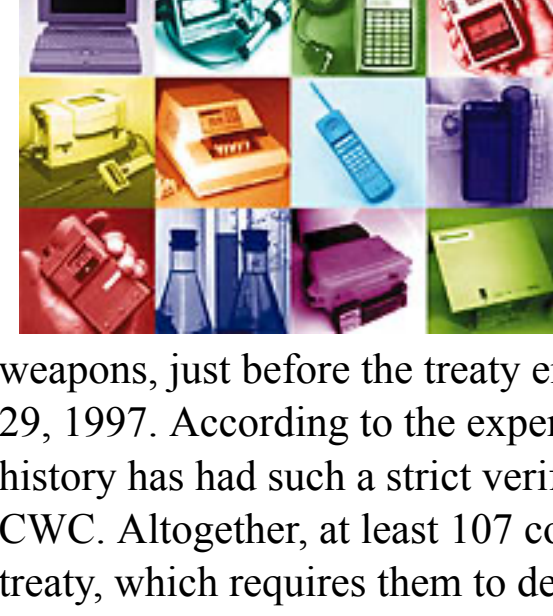


The Chemical Weapons Convention redefines "analytical challenge"

Strict treaty verification regimes necessitate an explosion of new arms control technology.



After much negotiation, the United States ratified the Chemical Weapons Convention (CWC), a multilateral treaty that prohibits the production, storage, and use of chemical weapons, just before the treaty entered into force on April 29, 1997. According to the experts, no other treaty in history has had such a strict verification regime as the CWC. Altogether, at least 107 countries have ratified the treaty, which requires them to declare all facilities that are capable of producing chemical weapons, regardless of whether they are actually being used for that purpose. Those with declared facilities are required to undergo routine on-site inspections to ensure that they are not producing, processing, or consuming chemical weapons. In addition, the treaty allows for international challenge inspections if one party suspects that another party is not playing by the rules. Developing appropriate methods for these on-site inspections has turned out to be a real analytical challenge.

OPCW--the keepers of the list

The Organization for the Prohibition of Chemical Weapons (OPCW), based in The Hague (The Netherlands), is the overseeing body responsible for implementation of the CWC. Ultimately the OPCW is in charge of the inspections--they decide what instrumentation and procedures will be used. So how did they come up with a list of equipment and analytical methods that would provide an adequate degree of intrusiveness for treaty verification yet not reveal proprietary information that could jeopardize the chemical industry? According to Lieutenant Colonel Dennis Perry, program manager for the U.S. Defense Special Weapons Agency's (DSWA) Chemical-Biological Arms Control Technology Program, before the CWC entered into force a preparatory commission was established to work out the details regarding what equipment would be used for the inspections and what procedures would be used for sampling as well as other issues that are not addressed in the treaty itself. "The whole issue of inspection equipment was one of considerable contention during the four-year period of the preparatory commission before the treaty entered into force," says Mike Moody of the Chemical and Biological Arms Control Institute, a nonprofit policy research organization that promotes arms control and nonproliferation issues. Nonetheless, after much debate, a list of equipment and procedures that OPCW inspectors are allowed to use during their inspection activities was finally agreed upon. Selected portions of the equipment list are given in Table 1.

Table 1. Selections from the list of OPCW-approved inspection equipment

Given the rate at which technology advances, alternative equipment and procedures that are faster and more cost-effective than those on the original list will undoubtedly surface. Will a debate ensue every time a change or addition is requested, or is there a well-defined process for making amendments to the list? According to Perry there is a provision in the treaty that sets up an advisory board of scientific experts who serve as technical advisors to the secretary general of the OPCW. Under the advisory board there are working groups, made up of scientists who periodically come to discuss new technology that may be used for treaty verification. "We are looking at new technology that would be better than what is currently available because there are some limitations in what is being used in the field now," says Perry. He and several other technical experts from his agency were heavily involved in the initial discussions regarding equipment and sampling issues for CWC verification. "We hope that we will be involved in planning the meetings with international experts to talk about issues regarding new technology."

Seeking faster sample prep

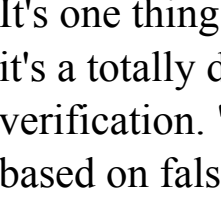
As prescribed in the treaty, when an inspection team arrives on site for a challenge inspection, they are allowed to stay for only a limited amount of time (up to 84 hours). It is therefore critical that the analyses be performed as quickly as possible. Samples can be taken from air, water, or soil; however, for these samples, GC/MS is the only approved on-site technology for determinative analysis, says Perry. The bottom line is that all samples must be prepared to go into a gas chromatograph, a process that takes much longer than any other step. "Many of the chemicals that are relevant to the treaty are well characterized; however, a lot of them are difficult to extract out of their matrices. We have been working on wet chemistry methods for more rapid sample preparation," explains Perry.

Rather than use standard preparation methods, which require centrifugation and extensive drying procedures, Perry and his colleagues are exploring supercritical fluid extraction (SFE) to save time. They have built a field-portable SFE unit that is compact, weighs only about 30 lb, and uses dry ice so that there is no need to bring a compressed CO₂ tank on site. This is important because inspectors must bring their own equipment with them--nothing is provided at a site for their use. "We are looking for technology that doesn't require heavy logistic support," emphasizes Perry. The portable SFE system is currently undergoing tests at Pacific Northwest National Laboratory to examine how various modifiers added to the CO₂ stream affect the extraction process. The unit performs well for the extraction of nonpolar analytes; however, polar analytes--particularly those found in soil matrices--are much more of a challenge, says Perry. He believes that if the right modifiers are identified, some of the more difficult analytes can be extracted from soil samples.

Perry's agency has been working with VERIFIN, the Finnish National Laboratory for CWC verification, to develop a joint sample preparation method, which is currently being used by the OPCW for training for on-site analyses. "There hasn't been an opportunity to use the method in the real sense, because there have been no challenge inspections yet," says Perry. Other laboratories around the world are also working to develop faster analytical methods for the determination of more than 330,000 CWC-related compounds (*Anal. Chem.* **1998**, *70*, 21 A, 246 A). Several of these laboratories have participated in round-robin proficiency testing, in which they analyze unknowns containing any number of chemical warfare (CW) agents and their degradation products--all for the purpose of becoming an OPCW-designated CWC verification laboratory. Because the treaty states that analyses can be performed on site, the ability to bring equipment out into the field has become a priority for many analysts. As a result, there have been numerous efforts to create modular laboratories that are rugged and compact enough to travel around the world (*Anal. Chem.* **1998**, *70*, 21 A, 23 A).

Where the best samples are

Because only a limited number of samples can be prepared for GC/MS analysis in the time allotted for an inspection, it is crucial that they are truly representative samples. Perry's group is therefore interested in looking for types of analyses that will provide an indication of where to sample. "We are looking for very quick, cheap, fairly sensitive technology (e.g., microspot tests and paper test strips that rely on colorimetric changes) that will give us a real 'go/no go' type of answer," says Perry. "If we think there is nothing there, then we can pass on to the next sample. We are always looking for a system that will point us to the problem areas."



Dennis Perry

Perry explains that the hand-held devices used in military field applications, such as the M8 chemical agent alarm, are not as well-suited for verification purposes because they suffer from interference problems that may lead to false positives. It's one thing to have false positives in the battlefield, but it's a totally different story in the area of treaty verification. "You cannot put the blame on someone based on false information. We are looking for a very low false-positive rate," he says. "We are willing to accept a few more false positives at the screening level because we assume that we will pick those up when we do GC/MS," adds Cathleen Hoefler, senior project manager for the DSWA's Chemical-Biological Arms Control Technology Program. "The whole idea with screening is so we don't end up wasting a lot of time preparing samples for GC/MS when they don't have anything in them. The idea is to eliminate those samples with a quick screening method so that we devote the GC/MS time to samples that are likely to contain something relevant." Given the large area that might be under investigation, it is questionable whether the objective will be met if there is time to analyze only one or two samples. "Not only are you trying to increase the number of samples that can be analyzed, but you have to ensure that the ones you do are the best ones," emphasizes Hoefler.

One of the key problems that Perry and his colleagues face is salty matrices. "Many of the soil samples that we are interested in contain high concentrations of salt, either from the soil itself or from breakdown products that form salts, which make it very difficult to prepare them for GC/MS analysis. Rather than moving forward with the standard approach--which requires the use of many exchange cartridges to remove the salts, a time-consuming dry-down step, and derivatization of the product prior to GC analysis--we are looking at capillary electrophoresis as an alternative screening technique," says Margo Jackisch, senior chemist at the Center for Verification Research, who works closely with Perry and his agency. "We've had good results with CE, but the apparatus is much too large to be 'fieldable,'" she says. "We are now considering the newly developed microchip-based CE systems, but we are concerned that the salts will clog the channels on the miniature devices. If we could find a way to make them work, it would be a major breakthrough in screening for us."

"I think our ultimate goal is to get away from GC/MS because of all the sample preparation that it requires," says Perry. "That is a long way off because it requires changing the international community's mind about how to do on-site analysis. Everyone accepts GC/MS." Improvements, such as faster GC with time-of-flight MS are being investigated, but that does not eliminate the sample preparation problem. Perry says it is too early to propose alternatives to GC/MS; however, he did mention that they are moving forward in that area. "We need a leap-ahead technology, which we haven't found yet," he remarks.

Protecting the chemical industry

One of the biggest concerns that the chemical industry had with the CWC and its on-site analyses was that proprietary information would be revealed to the inspectors. The Chemical Manufacturers Association (CMA) was therefore heavily involved in the CWC negotiations. As a result of the CMA's efforts, a provision was included in the treaty stating that inspectors are not allowed to see anything that is irrelevant to the CWC. About three years ago, Perry's group took on the task of developing blinding software that would prevent instrument operators from seeing chromatogram and mass spectral data. They consulted with Steve Stein and other experts at the National Institute of Standards and Technology (NIST), who developed a working version of the software, which has been made available to all manufacturers of GC/MS systems. "The software takes the analyst out of the loop. It automatically identifies a compound and tells the operator whether it found a treaty relevant chemical," explains Perry. There are provisions that allow inspectors to go back and look at the data. "If they think they've found something, they can go back and look at the underlying data for confirmation. Typically, however, they do not actually see the spectra; what they see is information that says compound X was found or nothing was found."

According to Perry the software is generic in the sense that it can be used with any mass spectral database. "We just happened to use the OPCW database because they are the chemicals that we are looking for. The underlying algorithm, however, will work with any GC/MS system." Basically the software takes a spectrum and searches the database for a match. "The value of the software is that it is very consistent--you do not get different interpretations of the same spectra from different analysts," says Perry. "It's very reproducible from test to test, and the false positive rate is very, very low."

Although a working version of the chemical identification masking software is available, Perry and his colleagues are looking for ways to improve it. "We are working on different modules of it now to fill in retention indices for the spectra, which were not in the initial version," says Perry. Retention indices are necessary to distinguish between compounds that have similar mass spectra. For example, when chloropicrin (a compound that contains three chlorine groups with a carbon and a nitrate group) is ionized, the nitrate group is knocked off and you are left with three chlorines attached to a carbon. It would appear as if you have chloroform or carbon tetrachloride with a missing chlorine. However, when retention indices are used, it becomes clear that the compound is indeed chloropicrin because it does not elute from the GC column at the same time as chloroform or carbon tetrachloride, explains Jackisch.

Another aspect of the software that is currently being improved involves the area of internal QA/QC. "If you don't find anything in a run, do you know if the instrument was really running properly during that run, or did it really not find anything?" asks Perry. To answer that question, he and his co-workers have added another part to the software that will signal to the operator when a run has been successfully completed.

Assessing and destroying stockpiles

The CWC requires all parties to make detailed declarations of their stockpiles; that is, all parties must declare how many chemical weapons they have in storage. In addition, all parties must completely eliminate their stockpiles over the next 10 years (a five-year extension period may be requested in some cases). The inspectors have the right to verify the declarations and ensure that progress is being made in the destruction of the weapons. How do they verify what is stored in a sealed artillery shell without taking a sample? Several nondestructive technologies have been investigated for this purpose, eliminating the need to physically remove toxic chemicals from their containers. Acoustic resonance spectroscopy (ARS) and portable isotopic neutron spectroscopy (PINS) are two technologies that have been examined, both of which are now commercially available. The newest, and probably the most promising technology, swept frequency acoustic interferometry (SFAI) (*Anal. Chem.* **1997**, *69*, 657 A), is still under development and about one year away from being completed, says Perry.

ARS is a relatively fast method; however, it is limited in that it requires a matching template--all compounds of interest have to have been previously detected and their resulting data must be stored in memory. In other words, an ARS system cannot analyze something it has not seen before. In contrast to ARS, which requires a template, SFAI uses a database of physical properties of chemicals, such as viscosity, density, and attenuation of sound, all of which can be found in the literature. In SFAI, a pulse of sound is sent out over a wide frequency and gets returned off the back wall of the container. The various properties are then compared with those in the database to determine if there is a match. SFAI is very fast (about 20 s per analysis), as opposed to PINS, which has a radiological source and takes about 1000 s, says Perry.

The challenges ahead

Although chemical weapons have been around for several decades, many questions remain regarding their environmental fate and their breakdown products, says Hoefler. It wasn't until arms control became an issue that the focus changed from simply understanding the chemistry of the agents themselves to better understanding what they become once they are released into the environment. The challenges that face analytical chemists involved in the identification of CW agents and their degradation products are enormous, adds Jackisch. "Every day we continue searching for technology that is faster, cheaper, and better. We have techniques that work, but they are painfully slow and laborious. We know that they can't be the long-term solution." Those who believe there is nothing left to do in the area of chemical weapons detection should think again--the war against chemical weapons is far from over.

Britt Erickson

